

Amendments to the Claims

Please cancel claim 1 without prejudice. Please add new claims 2-40

Listing of the Claims:

1. (canceled)
2. (new) A method of providing a population of recombined nucleic acids, the method comprising:
 - (i) providing a population of oligonucleotides comprising at least one set of codon-varied oligonucleotides, wherein at least one member of the set of codon-varied oligonucleotides is chemically synthesized using at least trinucleotide sequences and wherein two or more members of the population comprise overlapping oligonucleotides;
 - (ii) hybridizing at least two of the overlapping oligonucleotides to each other to provide a population of hybridized overlapping oligonucleotides, which population of hybridized overlapping oligonucleotides comprises at least one codon-varied oligonucleotide; and,
 - (iii) elongating members of the population of hybridized overlapping oligonucleotides, thereby providing the population of recombined nucleic acids.
3. (new) The method of claim 2, further comprising selecting at least first and second nucleic acids to be recombined, wherein the set of codon-varied oligonucleotides comprises a plurality of codon-varied nucleic acids which correspond to the first and second nucleic acids.
4. (new) The method of claim 3, wherein the first and second nucleic acids are homologous.
5. (new) The method of claim 3, wherein the first and second nucleic acids are non-homologous.
6. (new) The method of claim 2, wherein the providing step comprises trinucleotide synthesis

comprising:

- (a) providing a substrate sequence having a 5' terminus and at least one base, the 5' terminus and at least one base having protecting groups thereon;
- (b) removing the 5' protecting group of the substrate sequence to provide a 5' deprotected substrate sequence;
- (c) coupling the 5' deprotected substrate sequence with a selected trinucleotide phosphoramidite sequence having a 3' terminus, a 5' terminus, and three base groups, the 3' terminus, the 5' prime terminus, and the three base groups having protecting groups thereon, thereby yielding an extended oligonucleotide sequence; and,
- (d) repeating steps (b) and (c), wherein the extended oligonucleotide sequence yielded by each repeated step (c) becomes the substrate sequence of the next repeated step (b) until a desired codon-varied oligonucleotide is obtained.

7. (new) The method of claim 2, wherein the providing step comprises trinucleotide synthesis performed in an automated synthesizer which automatically performs the steps of:

- (a) providing a substrate sequence having a 5' terminus and at least one base, the 5' terminus and at least one base having protecting groups thereon;
- (b) removing the 5' protecting group of the substrate sequence to provide a 5' deprotected substrate sequence;
- (c) coupling the 5' deprotected substrate sequence with a selected trinucleotide phosphoramidite sequence having a 3' terminus, a 5' terminus, and three base groups, the 3' terminus, the 5' prime terminus, and the three base groups having protecting groups thereon, thereby yielding an extended oligonucleotide sequence; and,
- (d) repeating steps (b) and (c), wherein the extended oligonucleotide sequence yielded by each repeated step (c) becomes the substrate sequence of the next step (b) until a desired codon-varied oligonucleotide is obtained.

8. (new) The method of claim 7, the method further comprising inputting character string information into the automatic synthesizer corresponding to the desired codon-varied

oligonucleotides to be obtained.

9. (new) The method of claim 8, wherein the character string information corresponds to two or more nucleic acids to be recombined.

10. (new) The method of claim 2, wherein the providing step comprises providing a substrate sequence having a 5' terminus and at least one base, the 5' terminus and at least one base having protecting groups thereon, the substrate sequence further comprising a 3' end that is covalently attached to a solid support.

11. (new) The method of claim 2, wherein the providing step comprises coupling together one or more of: mononucleotides, trinucleotide phosphoramidite sequences, and oligonucleotides.

12. (new) The method of claim 2, wherein the providing step comprises split-pool synthesis comprising:

- (a) providing substrate sequences, each having a 5' terminus and at least one base, the 5' terminus and at least one base having protecting groups thereon;
- (b) removing the 5' protecting groups of the substrate sequences to provide 5' deprotected substrate sequences;
- (c) coupling the 5' deprotected substrate sequences with a population of a selected trinucleotide phosphoramidite sequence, each having a 3' terminus, a 5' terminus, and three base groups, the 3' terminus, the 5' terminus, and the three base groups having protecting groups thereon, thereby yielding extended oligonucleotide sequences;
- (d) repeating steps (b) and (c), wherein the extended oligonucleotide sequences yielded by each step (c) become the substrate sequences of the next step (b), until extended intermediate oligonucleotide sequences are produced;
- (e) splitting the extended intermediate oligonucleotide sequences into two or more separate pools;
- (f) removing the 5' protecting groups of the extended intermediate oligonucleotide sequences to

provide 5' deprotected extended intermediate oligonucleotide sequences in the two or more separate pools;

(g) coupling the 5' deprotected extended intermediate oligonucleotide sequences with one or more selected mononucleotides, trinucleotide phosphoramidite sequences, or oligonucleotides in the two or more separate pools, thereby yielding further extended intermediate oligonucleotide sequences;

(h) pooling the further extended intermediate oligonucleotide sequences from the two or more separate pools into a single pool; and,

(i) repeating steps (b) through (h), wherein the further extended intermediate oligonucleotide sequences in the single pool of each step (h) become the substrate sequences of the next step (b), until desired codon-varied oligonucleotides are obtained.

13. (new) The method of claim 12, further comprising selecting at least first and second nucleic acids to be recombined, wherein the set of codon-varied oligonucleotides comprises a plurality of codon-varied nucleic acids which correspond to the first and second nucleic acids wherein the first and second nucleic acids are non-homologous and are synthesized using the split-pool synthesis format.

14. (new) The method of claim 13, wherein the non-homologous first and second nucleic acids are less than 90 percent identical.

15. (new) The method of claim 14, wherein the split-pool synthesis format is module-based with a smallest module being a single trinucleotide in length and a larger module being at least 15 nucleotides in length.

16. (new) The method of claim 2, wherein the providing step comprises split-pool synthesis performed in an automated synthesizer which automatically performs the steps of:

(a) providing substrate sequences having a 5' terminus and at least one base, the 5' terminus and at least one base having protecting groups thereon;

- (b) removing the 5' protecting groups of the substrate sequences to provide 5' deprotected substrate sequences;
- (c) coupling the 5' deprotected substrate sequences with a population of a selected trinucleotide phosphoramidite sequence having a 3' terminus, a 5' terminus, and three base groups, the 3' terminus, the 5' terminus, and the three base groups having protecting groups thereon, thereby yielding extended oligonucleotide sequences;
- (d) repeating steps (b) and (c), wherein the extended oligonucleotide sequences yielded by each step (c) become the substrate sequences of the next step (b), until extended intermediate oligonucleotide sequences are provided;
- (e) splitting the extended intermediate oligonucleotide sequences into two or more separate pools;
- (f) removing the 5' protecting groups of the extended intermediate oligonucleotide sequences to provide 5' deprotected extended intermediate oligonucleotide sequences in the two or more separate pools;
- (g) coupling the 5' deprotected extended intermediate oligonucleotide sequences with one or more selected mononucleotides, trinucleotide phosphoramidite sequences, or oligonucleotides in the two or more separate pools, thereby yielding further extended intermediate oligonucleotide sequences;
- (h) pooling the further extended intermediate oligonucleotide sequences from the two or more separate pools into a single pool; and,
- (i) repeating steps (b) through (h), wherein the further extended intermediate oligonucleotide sequences in the single pool of each step (h) become the substrate sequences of the next step (b), until desired codon-varied oligonucleotides are obtained.

17. (new) The method of claim 16, further comprising selecting at least first and second nucleic acids to be recombined, wherein the set of codon-varied oligonucleotides comprises a plurality of codon-varied nucleic acids which correspond to the first and second nucleic acids wherein the first and second nucleic acids are non-homologous and are synthesized using the split-pool synthesis format performed in an automated synthesizer.

18. (new) The method of claim 17, wherein the non-homologous first and second nucleic acids are less than 90 percent identical.

19. (new) The method of claim 18, wherein the split-pool synthesis format performed in an automated synthesizer is module-based with a smallest module being a single trinucleotide in length and a larger module being at least 15 nucleotides in length.

20. (new) The method of claim 16, the method further comprising inputting character string information into the automatic synthesizer corresponding to the desired codon-varied oligonucleotides to be obtained.

21. (new) The method of claim 20, wherein the character string information corresponds to two or more nucleic acids to be recombined.

22. (new) The method of claim 16, wherein the providing step further comprises providing a substrate sequence having a 3' terminus covalently attached to a solid support.

23. (new) The method of claim 2, wherein the hybridizing step occurs in vitro.

24. (new) The method of claim 2, wherein the hybridizing step occurs in vivo.

25. (new) The method of claim 2, wherein (iii) comprises elongating the one or more members of the population of hybridized overlapping codon-varied oligonucleotides with a polymerase.

26. (new) The method of claim 25, wherein the polymerase is a thermostable polymerase.

27. (new) The method of claim 2, the method further comprising:
denaturing the population of recombined nucleic acids to provide a set of denatured recombined

nucleic acids;

re-hybridizing at least one member of the set of denatured recombined nucleic acids to at least one other member of the set of denatured recombined nucleic acids to provide a population of re-hybridized recombined nucleic acids;

elongating one or more members of the population of rehybridized recombined nucleic acids to provide a population of further recombined nucleic acids; and,

selecting at least one member of the population of further recombined nucleic acids for at least one desired trait or property.

28. (new) The method of claim 2, the method further comprising the steps of:

denaturing the population of recombined nucleic acids to provide a set of denatured recombined nucleic acids;

re-hybridizing at least one member of the set of denatured recombined nucleic acids to at least one other member of the set of denatured recombined nucleic acids to provide a population of re-hybridized recombined nucleic acids;

elongating one or more members of the population of re-hybridized recombined nucleic acids to provide a population of further recombined nucleic acids; and,

repeating the denaturing, re-hybridizing and elongating steps at least once.

29. (new) The method of claim 28, further comprising selecting at least one member of the population of further recombined nucleic acids for at least one desired trait or property.

30. (new) The method of claim 28, wherein a plurality of members of the population of recombined nucleic acids are selected for a desired trait or property to provide first round selected nucleic acids, the method further comprising:

hybridizing at least one member of a second set of overlapping codon-varied oligonucleotides to at least one other member of the second set of overlapping codon-varied oligonucleotides to provide a second population of hybridized overlapping codon-varied oligonucleotides, which second set of overlapping codon-varied oligonucleotides is derived from the first round selected

nucleic acids; and,

elongating one or more members of the second population of hybridized overlapping codon-varied oligonucleotides to provide a second population of further recombined nucleic acids.

31. (new) The method of claim 30, further comprising sequencing the first round selected nucleic acids, wherein the second set of overlapping codon-varied oligonucleotides is derived from the first round selected nucleic acids by aligning sequences of the first round selected nucleic acids to one another to identify regions of similarity and regions of diversity in the first round selected nucleic acids, and synthesizing the second set of overlapping codon-varied oligonucleotides to comprise a plurality of oligonucleotides, each of which comprise subsequences corresponding to at least one region of diversity.

32. (new) The method of claim 30, wherein the first round selected nucleic acids encode polypeptides of about 50 amino acids or less.

33. (new) The method of claim 30, wherein the second set of overlapping codon-varied oligonucleotides comprises a plurality of oligonucleotide member types which comprise consensus region subsequences derived from a plurality of the first round selected nucleic acids.

34. (new) The method of claim 2, further comprising selecting at least one member of the population of recombined nucleic acids for at least one desired trait or property.

35. (new) The method of claim 2, wherein the set of overlapping codon-varied oligonucleotides comprises a plurality of oligonucleotide member types which comprise consensus region subsequences derived from a plurality of homologous target nucleic acids.

36. (new) The method of claim 2, wherein the set of overlapping codon-varied oligonucleotides comprises at least 3 oligonucleotide member types.

37. (new) The method of claim 36, wherein the set of overlapping codon-varied oligonucleotides comprises at least 5 oligonucleotide member types.

38. (new) The method of claim 37, wherein the set of overlapping codon-varied oligonucleotides comprises at least 10 oligonucleotide member types.

39. (new) The method of claim 2, wherein the set of overlapping codon-varied oligonucleotides comprises a plurality of homologous oligonucleotide member types, wherein the homologous oligonucleotide member types are present in equimolar amounts.

40. (new) The method of claim 2, wherein the set of overlapping codon-varied oligonucleotides comprises a plurality of homologous oligonucleotide member types, wherein the homologous oligonucleotide member types are present in non-equimolar amounts.